REMARKS

Claims 1-38 were pending the application. Claims 2, 3, 8, 9, and 17-38 have been canceled, without prejudice, claims 1, 4, 5, 6, 7, 13, 15, and 16 have been amended, and new claims 39, 40, 41, and 42 have been added. Accordingly, upon entry of this amendment, claims 1, 4-7, 10-16, and 39-42 will remain pending.

Support for the amendments to the claims and the new claims may be found throughout the specification, including the originally filed claims. Support for the amendments to claims 5 and 6 may be found at, for example, Table 1 of Applicants specification. Support for the amendment to claim 7 may be found in Applicants' specification at least, for example, at page 25, line 18.

No new matter has been added. Any amendments to the claims was done solely to more particularly point out and distinctly claim the subject matter of Applicants' invention in order to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Election/Restrictions

With respect to the Restriction Requirement, the Examiner has stated that "claim 37, which was originally separated from the claims of the elected Group I, has been placed with those claims of the elected Group I."

Priority

Applicants thank the Examiner for acknowledging Applicants' claims of priority to U.S. Provisional application 60/144,448, filed July 16, 1999 and U.S. Provisional application 60/149,402, filed August 17 1999, the entire contents of which are incorporated into the instant application by reference.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information

submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

No information disclosure statement is currently associated with this application.

Applicants respectfully submit that they intend to file an Information Disclosure Statement for the instant application in due course.

Specification

The Examiner has objected to the disclosure because "[o]n page 28, lines 11-14, of the specification applicants state "As used herein, the term 'hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other..." Such a statement that nucleotide sequences which are 60% homologous would hybridize under stringent conditions is considered to be repugnant to what is known in the art."

Applicants respectfully traverse the foregoing objection to the specification. Applicants respectfully submit that the above statement is not repugnant to what is known in the art as evidenced by, for example, U.S. Patent No. 6,436,684, attached hereto as Appendix A. At column 26, lines 11-15, U.S. Patent No. 6,436,684 states that "[a]s used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences encoding a peptide ***at least 60-70% homologous*** to each other typically remain hybridized to each other." Therefore, Applicants respectfully submit that this statement was acceptable to those of ordinary skill in the relevant art at the time the application was filed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing objection to the specification.

Claim Objections

The Examiner has objected to claims 1-17 and 36-38 because "claim 2 recites "RRP protein". It is suggested that the first time such a reference is made it be written out in full followed by the abbreviation in parenthesis, i.e. "DNA replication, ribosome and pathogenesis (RRP) protein"."

Applicants respectfully traverse the foregoing objection to claim 2. However, in the interest of expediting prosecution, claim 2 has been cancelled thereby rendering the foregoing objection moot.

The Examiner has also objected to claim 13 because it "recites "said cell...". It is suggested that this be amended to "said host cell..."."

Applicants respectfully traverse the foregoing objection to claim 13. However, in the interest of expediting prosecution of the instant application, and in no way acquiescing to the Examiner's objection, Applicants have amended claim 13 as suggested by the Examiner.

The Examiner has also objected to claims 1-17 and 36-38 as comprising nonelected subject matter "i.e. SEQ ID NOs: 5, 9, 11, 13, 15, 19, 21, 23, and 27 and the 'nucleic acid molecules set forth in Appendix A'".

Applicants respectfully traverse the foregoing objection to the claims. However, in the interest of expediting prosecution, claims 2, 3, 8, 9, and 17-38 have been canceled and claims 1, 4, 5, 6, and 7 have been amended to refer to elected subject matter. Accordingly, Applicants respectfully request withdrawal of the foregoing objection to the claims.

Rejection of Claims 2 and 8 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 2 and 8 under 35 U.S.C. §112, second paragraph, as being indefinite for "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution of the instant application, Applicants have canceled claims 2 and 8, thereby obviating the Examiner rejection to these claims.

Rejection of Claims 5-9 and 36-38 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 5-9 and 36-38 under 35 U.S.C. §112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of the opinion that

> [t]he specification, however, only provides a single representative species isolated from *Corynebacterium glutamicum* encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these nucleic acid molecules by any identifying structural characteristics or properties. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. It is noted that applicants claims read on a genus of nucleic acid molecules and host cells comprising said nucleic acid molecules, wherein the nucleic acid molecules have no functional limitations, relatively minor structural limitations and thus absolutely no structure to function/activity relationship.

Applicants have canceled claims 8, 9, and 36-38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 5-7, and new claims 39, 40, and 41, Applicants respectfully traverse the foregoing rejection and submit that there is sufficient written description in Applicants' specification regarding nucleic acid molecules comprising SEQ ID NO:1 and nucleic acid molecules with a significant degree of homology to SEQ ID NO:1 and SEQ ID NO:2, which encode polypeptides which are capable of functioning as extracellular nucleases, to inform a skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed as required by section 112, first paragraph (see M.P.E.P. 2163.02). In order to meet the written description requirement of the first paragraph of 35 U.S.C. §112, it is not necessary that a patent specification describe each and every specific member of a genus recited in a claim.

With respect to the remaining rejected claims 5-7, and new claims 39, 40, and 41, a claim to a genus of chemical compounds satisfies the written description requirement when its accompanying specification either defines by sequence a representative number of its members falling within the scope of the genus or when its accompanying specification defines the structural features common to a substantial portion of the genus *(The Regents of the University of California v. Eli Lilly and Co.,*

43 USPQ2d 1398, 1406 (Fed. Cir. 1997)). For reasons discussed in detail below, the instant specification satisfies this requirement for the claimed invention.

The instant specification describes how modified or disrupted variants of SEQ ID NO:1 may be identified or produced and teaches what kind of sequence variation functional and non-functional variants of a polypeptide encoded by SEQ ID NO:1 may have (see, for example, page 27, line 28 through page 30, line 19).

Furthermore, claim 5 is not directed to any and/or all polynucleotides but rather is directed only to those which encode functional extracellular nucleases that are encoded by a nucleic acid molecule with a high degree of identity to SEQ ID NO:1 and which hybridizes to a full complement of a nucleic acid molecule consisting of SEQ ID NO:1, in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C. The recited stringent hybridization conditions determine a specific subgenus of molecules in accordance with the invention, *i.e.*, the subgenus of polynucleotides that encode polypeptides capable of functioning as extracellular nucleases.

Example 14 of the *Revised Interim Written Description Guidelines Training Materials* provides that a claim directed to variants of a polypeptide having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity."

Similarly, in the present case, claims 6 and 41 are directed to isolated nucleic acid molecules comprising or consisting of a nucleotide sequence that is at least 90% identical to the nucleotide sequence shown in SEQ ID NO:1, wherein the nucleotide sequence encodes a polypeptide capable of functioning as an extracellular nuclease.

Applicants have disclosed in the instant specification assays for identifying all of the at least 90% identical variants of SEQ ID NO:1 which encode polypeptides capable of functioning as extracellular nucleases (see, for example, page 27, line 28

through page 30, line 19 and Example 8 at page 56, lines 4-31 of Applincants' specification). Thus, based on the teachings in Applicants' specification, one of skill in the art would conclude that Applicants were in possession of the claimed invention at the time of filing.

With respect to claim 7, which is directed to an isolated nucleic acid molecule which encodes a polypeptide fragment comprising at least 25 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2, Applicants have described various fragments of the polynucleotides of the invention.

In Example 15 of the *Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, First Paragraph Written Description Requirement* the "theoretical specification" discloses a messenger RNA sequence, SEQ ID NO:1, which encodes a human growth hormone. The "theoretical specification" claims antisense molecules that inhibit the production of human growth hormone. The Guidelines provide that

> [c]onsidering the specification's disclosure of (1) ***the sequence (SEQ ID NO:1) which defines and limits the structure of any effective molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim*** and 2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with, 3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention.....***the claimed invention is adequately described.***

Similar to Example 15 of the *Interim Guidelines*, the instant specification describes the nucleotide sequence of the nucleic acid molecules of the invention (SEQ ID NO:1) ***which define and limit the structure of any nucleotide fragments such that one skilled in the art would be able to immediately envisage members of the genus embraced by the nucleotide fragment claims.***

Moreover, as provided in Example 15 of the *Interim Guidelines*, the generation of oligonucleotide fragments is routine. For example, (as indicated in Example 15 of the *Interim Guidelines*) any specified fragment can be ordered from a commercial synthesizing service. Finally, Applicants' specification teaches how such polynucleotide fragments encoding polypeptides may be tested for activity (see, for

example, page 42, lines 11-24 and Example 8, at page 56, lines 4-31 of Applincants' specification).

Based on the foregoing teachings in Applicants' specification and the knowledge generally available in the art, one skilled in the art would conclude that Applicants were in possession of the claimed invention at the time of filing of the application. The skilled artisan would also be able to make and use the claimed polypeptide fragments using only routine experimentation.

Accordingly, based on the amendments to the claims and the comments set forth above, Applicants respectfully request reconsideration and withdrawal of the instant rejection under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 1-17 and 36-38 Under 35 U.S.C. §101 and 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-17 and 36-38 under 35 U.S.C. §101 because "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility." In particular, the Examiner is of the opinion that

> The claimed nucleic acid molecules and host cells are not supported by a specific asserted utility because the disclosed use of the nucleic acid is generally applicable to any nucleic acid and therefore is not particular to the nucleic acid sequence being claimed. Further, the claimed nucleic acid molecule is not supported by a substantial utility because the specification states only that the nucleic acid molecules are useful for the identification of microorganisms which can be used to produce fine chemicals, the modulation of fine chemical production in C. glutamicum or related bacteria, the typing or identification of C. glutamicum or related bacteria, as reference points for the mapping the C. glutamicum genome and as markers for transformation. A starting material that can only be used to produce a final product does not have a substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the encoded proteins that are to be produced as final products resulting from processes involving the claimed nucleic acid molecules have asserted or identified specific and substantial utilities. The research contemplated by applicants to characterize potential ligand and protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of the encoded proteins or associated ligands or the mechanism in which proteins or ligands

> are involved in the production of fine chemicals does not define a "real world" context of use. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid molecules such that another non-asserted utility would be well established for the compounds.

Applicants have canceled claims 2, 3, 8, 9, and 17-38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 1, 4-7, 10-16, and 39-42, Applicants respectfully traverse the foregoing rejection and assert that a specific, substantial and well-established utility, which would have been credible to one skilled in the art at the time of the invention, is clearly disclosed in the instant specification.

Claims 1 and 39 are directed to an isolated nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. Claims 4 and 40 are directed to an isolated nucleic acid molecule which encodes a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO:2, or a complement thereof. Claim 5 is directed to an isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a Corynebacterium glutamicum polypeptide comprising the amino acid sequence of SEQ ID NO:2 wherein the nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:1 in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C, and wherein said nucleic acid molecule encodes a polypeptide which is capable of functioning as an extracellular nuclease. Claims 6 and 41 are directed to an isolated nucleic acid molecule comprising or consisting of a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as an extracellular nuclease. Claim 7 is directed to an isolated nucleic acid molecule comprising a fragment of at least 25 nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof.

The cited utilities in the specification include modulation of chemical production and using the proteins to produce fine chemicals. Applicants respectfully submit that these utilities are credible. Applicants' respectfully submit that

Applicants asserted utilities are also specific and substantial. The molecules described in Applicants' specification are DNA replication, ribosome and pathogenesis (RRP) molecules. In particular, SEQ ID NO:1 encodes an extracellular nuclease (see Table 1 of Applicants' specification). The claimed polynucleotides and polypeptides, *e.g.,* the sequences of SEQ ID NO:1 and SEQ ID NO:2, have extracellular nuclease protein activity as described in the instant application. Applicants have described the chemical, physical and the functional characteristics of the RRP polypeptides, *e.g.,* the extracellular nuclease polypeptides of the invention, in the instant specification, including, for example, page 7, line 32 through page 8, line 8, page 14, line 16 through page 19, line 2, and in Table 1. Furthermore, the activity of extracellular nucleases were well-known by one of ordinary skill in the art at the time the application was filed.

As the Examiner is aware, the applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965). Instead, evidence will be sufficient, if considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. M.P.E.P. §2164.07. Based on the teachings in Applicants' specification regarding the activity of the molecules used in the methods of the invention, Applicants respectfully submit that a person of ordinary skill in the art would conclude that Applicants' asserted utility is more likely than not true, which is all that is required under 35 U.S.C. §101.

In view of the foregoing, Applicants asserts that the utilities set forth in the specification for the invention as instantly claimed are specific, credible and substantial and/or well-established utilities that would have been recognized as such by one of skill in the art at the time the application was filed. Therefore, the instant claims meet the requirements of 35 U.S.C. §101, and Applicants respectfully request reconsideration and withdrawal of this rejection.

In addition, the Examiner has rejected claims 1-17 and 36-38 under 35 U.S.C. §112, first paragraph, as "failing to comply with the enablement requirement." In particular, the Examiner is of the opinion that "as discussed above under the rejection under 35 U.S.C. §101, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention."

Applicants respectfully traverse the foregoing rejection. As set forth above, Applicants' specification sets forth at least one specific, substantial and well-established utility, which would have been credible to one skilled in the art at the time of the invention. Therefore, one of ordinary skill in the art would clearly know how to make and use the claimed invention. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 7-9 Under 35 U.S.C. §102(e)

The Examiner has rejected claims 7-9 under 35 U.S.C. §102(e) as being anticipated by Rubenfield et al. (U.S. Patent No. 6,551,795 B1). In particular, the Examiner is of the opinion that "Rubenfield et al. teach an isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of the nucleotide sequence of SEQ ID NO: 1, which comprises at least 17 contiguous residues of SEQ ID NO: 1 (see specifically residues 217-233 of instantly disclosed SEQ ID NO: 1 compared to residues 1874 through 1895 of SEQ ID NO: 3845 of U.S. Patent No. 6,551,795 B1). Further the taught nucleic acid molecule of Rubenfield et al. would hybridize to itself under stringent conditions and comprises at least a portion thereof the nucleic acid molecule of claim 1, as a single nucleotide is a portion of SEQ ID NO: 1."

Applicants respectfully traverse the foregoing rejection of claims 7-9. However, in order to expedite prosecution of the instant application, and in no way acquiescing to the Examiner's rejection, claims 8 and 9 have been canceled, thereby rendering the foregoing rejection moot as it pertains to these claims.

For a prior art reference to anticipate a claimed invention, the prior art must teach each and every element of the claimed invention. *Lewmar Marine v. Barient* 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

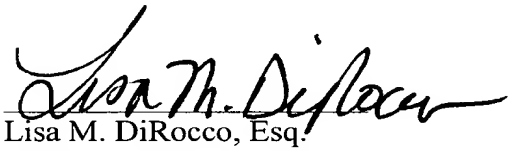
With respect to claim 7, Applicants respectfully submit that Rubenfield et al. (U.S. Patent No. 6,551,795 B1) does not disclose a nucleotide sequence encoding a polypeptide fragment comprising ***at least*** 25 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1. Therefore, Rubenfield et al. do not teach each and every limitation of claim 7. Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant 35 U.S.C. §102(b) rejection.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP



Lisa M. DiRocco, Esq.
Registration No. 51,619
Attorney for Applicants

28 State Street
Boston, MA 02109
Tel. (617) 227-7400

Dated: **March 24, 2004**